knock down Zic2a and Zic5 function, consistent with a requirement for zics during NC formation in zebrafish. Temporal analysis of NC marker expression in zic2a and zic5 morphants has revealed a migratory defect. This migratory phenotype is also present in embryos depleted for another member of the zic family, zic2b. Live imaging studies, currently in progress, will pinpoint the stage of NC development which requires Zics. These studies will define specific roles for zic genes during neural crest induction, maintenance, and/or migration, and will serve as a basis for dissecting the mechanism of zic gene function in the vertebrate neural crest.

doi:10.1016/j.ydbio.2009.05.502

Program/Abstract # 475
Conditional ablation of Dlx3 in cranial neural crest-derived cells results in abnormal development of hair, teeth and craniofacial bone

Olivier Duverger, Nicole B. Gentile,
Katherine M. Maddox, Maria I. Morasso
Developmental Skin Biology Section, NIAMS, NIH, Bethesda, MD, USA

During embryogenesis, the homeodomain transcription factor, Dlx3, is involved in the development of structures derived from epithelial–mesenchymal interactions such as hair and teeth, as well as in bone (craniofacial and appendicular). In humans, a frameshift mutation in the coding sequence of DLX3 results in an ectodermal dysplasia known as Tricho-Dento-Osseous (TDO) syndrome. TDO patients have defects in hair, teeth and bone. At E11.5, Dlx3 is expressed in post-migratory cranial neural crest cells (CNC) that are known to contribute to hair, teeth and craniofacial bone formation. In order to assess the role of Dlx3 in CNC, we generated mice lacking Dlx3 in all CNC-derived tissues, using Wnt1-cre and Dlx3-floxed mice. These mice exhibit visible hair defects with a disheveled coat, kinky vibrissae and sparse hair on the head. Analysis of the composition of the coat revealed a change in the proportion and structure of specific hair types. Mutant mice also exhibit major tooth defects: their incisors are small and underdeveloped as compared to their wild-type littermates. Histological analysis of the teeth revealed a dramatic hypoplasia of the dentine that is totally absent on the labial part of the incisors. The structure, size and bone mineral density of the skull are also affected. These data demonstrate that the expression of Dlx3 in CNC-derived cells is essential for normal development of the three structures affected in TDO syndrome.

doi:10.1016/j.ydbio.2009.05.503

Program/Abstract # 476
Role of Dlx3 in hair cycling

Joonsung Hwang, Joung-Soo Kim, Jean Suh, Maria I. Morasso
[1]*Developmental Skin Biology Section, NIAMS, NIH, Bethesda, MD, USA*
[2]*Department of Dermatology, Hanyang University College of Medicine, Seoul, Republic of Korea*

Ectodermal appendages such as hair and tooth are attractive models for understanding the mechanisms underlying epithelial–mesenchymal interactions. Dlx3 belongs to the Distal-less family of homeodomain transcription factors, and an autosomal dominant mutation in *DLX3* is responsible for the ectodermal dysplasia termed Tricho-Dento-Osseous syndrome (TDO), characterized by defects in hair, tooth, and bone development. Recently, we assessed the function of Dlx3 as a crucial transcriptional regulator of hair formation and regeneration using a Cre-mediated knockout mouse model. The most striking defect in those mice was complete alopecia due to failure in hair morphogenesis and cycling. However, it is not clear that the failure of hair cycling is due to a direct result from Dlx3 loss or a secondary effect from an incomplete first anagen in the Cre-mediated knockout mouse. To further investigate the specific role of Dlx3 in the hair cycle, we are utilizing a tamoxifen-inducible system by crosses of K14-CreERT mice with Dlx3-floxed mice. Knockout of Dlx3 expression is accomplished by the topical application of tamoxifen during the first postnatal catagen, especially to avoid the cumulative effect from an incomplete hair cycle as mentioned above. Our preliminary results establish Dlx3 as an essential regulator of hair cycling, validated by the permanent hair loss in the inducible knockout mice.

doi:10.1016/j.ydbio.2009.05.504

Program/Abstract # 477
Aquaporin-3b and other direct targets of the Zic1 transcription factor

Jean Cornish, Anna Gerasimova, Christa Merzdorf
Department of Cell Biology and Neuroscience, Montana State University, Bozeman, MT, USA

Zic transcription factors cause multiple birth defects, among them the neural tube defect holoprosencephaly. We conducted a screen for direct targets of the Zic1 transcription factor, which plays multiple roles during early development, for example in patterning the early neural plate, development of the neural crest, and somite development. An aquaporin gene was identified in this screen, which we named aqp-3b due to its high similarity to aqp-3. aqp-3b and aqp-3 are both expressed in adult tissues of *Xenopus*, but only aqp-3b is expressed during embryonic development. In neurula stages, aqp-3b is expressed very specifically in the anterior neural folds, extending more posteriorly as the neural tube begins to close. Aquaporins are transmembrane proteins that form water channels in the plasma membrane and have been shown to facilitate cell movement and cell shape changes, which are both needed for neural tube closure. Our results suggest that aqp-3b morpholino oligonucleotides disrupt normal neural tube closure in *Xenopus* embryos, indicating that aqp-3b may be required for proper formation of the neural folds. Very few genes are known to be specifically involved in neural fold formation and we are examining the role of aqp-3b in this process further. Thus, aqp-3b may contribute to the mechanisms by which reduced activity of zic genes cause neural tube defects. Most recently, we identified another gene from our screen, which is also expressed in the neural folds. We are examining this gene further and will present our data.

doi:10.1016/j.ydbio.2009.05.505

Program/Abstract # 478
Identifying the functional domains of FoxD5, a neural fate specifying gene

Sally A. Moody, Pallavi Mhaske, Karen M. Neilson, Steven L. Klein
Department Anatomy and Regen Biol., GWU, Washington, DC, USA

FoxD5, an early-expressed neural transcription factor, is required for the appropriate expression of 11 other neural TFs; it up-regulates 3 TFs that promote an immature neural fate (gem, sox11, zic2), expands 2 TFs that maintain proliferative neural progenitors (sox2, sox3), and represses 6 TFs that promote the onset of neural differentiation (zic1, zic3, soxD, Xiro1–3). Using VP16-activating and EnR-repressing foxD5 constructs, we found that it regulates some NFS genes by transcriptional activation (gem, zic2) and others by transcriptional repression (zic1, zic3, Xiro1–3). These experiments, however, could not determine how the sox genes are regulated. Because FoxD5 contains several domains